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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,223	02/23/2004	Thomas Maciag	536895013CT1	3032

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DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
WOODWARD, CHERIE MICHELLE	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,223	MACIAG ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 14-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/21/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group III, claims 6-13, in the reply filed on 24 May 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL.

Claims 1-20 are pending. Claims 1-5 and 14-20 are withdrawn as being drawn to non-elected inventions. Claims 6-13 are under examination.

Priority/Benefit

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Provisional Application No. 60/314,837 (filed 24 August 2001), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The provisional application does not support or disclose the subject matter of the claims currently under examination. As such, benefit is denied to U.S. Provisional Application No. 60/314,837.

Benefit is granted to PCT/US02/27247, filed 26 August 2002, which does disclose the subject matter of the claims currently under examination.

Specification

3. The use of the trademark SPRAGUE DAWLEY (p. 48, line 13) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

4. The disclosure is objected to because of the following informalities:

a. There are numerous appearances of IL-1_ , IL-1□, or IL-1 [additional spaces following IL-1 and the next word] where it appears there should be a Greek symbol following "IL-1". It is unclear if these symbols are the result of typographical errors, computer software conversion problems, or some reason.

b. The chemical tetrathiomolybdate (TTM) is misspelled in the specification at page 5, line 10.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim recites administration of "an IL-1α release inhibiting amount of a copper chelator..." However, there is no indication in the disclosure of what amount of a copper chelator would be "an IL-1α release inhibiting amount" for any mammalian species. The claim, as written, does not define the metes and bounds of the amount of copper chelator to administer. For example, a toxic amount resulting in death, would meet the limitations of the claim, as written. Additionally, it is unclear from the claim, as written, whether he inhibition of the release of IL-1α is to encompass both traditional and non-traditional export of IL-1α or whether the release inhibition amount is limited to the inhibition of non-traditional export of IL-1α. Further, it is unclear whether "non-traditional release" refers to naturally occurring necrosis or cell leakage after a vessel wall injury.

7. Claim 9 recites the limitation "said mammal" in line 3. There is insufficient antecedent basis for this limitation in the claim. Claim 9 is an independent claim. There is no prior reference to a mammal in the claim such that the phrase "said mammal" has antecedent basis.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 6-9 and 11-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Cooper et al., US Patent 6,951,890 (4 October 2005, benefit to 12 March 2002).

The claims recite a method of inhibiting neointima formation following vessel injury in a mammal comprising administering to said mammal an IL-1α release inhibiting amount of a copper chelator, thereby inhibiting said neointima formation; a method of inhibiting macrophage infiltration following vessel injury in a mammal comprising administering an effective amount of a copper chelator; wherein said macrophage infiltration is associated with inflammation; a method of inhibiting cell proliferation associated with arterial wall injury comprising administering an effective amount of a copper chelator to said mammal, thereby inhibiting said cell proliferation; a method of inhibiting secretion of extracellular matrix following arterial wall injury in a mammal comprising inhibiting non-traditional export of at least one of FGF-1 and IL-1α from a cell at the site of said injury, and further wherein said export is inhibited by administering an effective amount of a copper chelator to said mammal thereby inhibiting said secretion of extracellular matrix in said mammal; a method of inhibiting neointimal thickening associated with arterial wall injury in a mammal comprising inhibiting non-traditional export of at least one of FGF-1 and IL-1α from a cell at the site of said injury and further wherein said export is inhibited by administering an effective amount of a copper chelator to said mammal, thereby inhibiting said neointimal thickening in said mammal; a method of inhibiting adventitial angiogenesis associated with arterial wall injury in a mammal, said method comprising inhibiting non-traditional export of at least one of FGF-1 and IL-1α from a cell at the site of said injury and further wherein said export is inhibited by administering an effective amount of a copper chelator to said mammal, thereby inhibiting said adventitial angiogenesis in said mammal; a method of inhibiting adventitial angiogenesis associated with arterial wall injury in a mammal, said method comprising inhibiting non-traditional export of at least one of FGF-1 and IL-1α from a cell at the site of said injury and further wherein said export is inhibited by

administering an effective amount of a copper chelator to said mammal, thereby inhibiting said adventitial angiogenesis in said mammal.

Cooper et al., teach methods for treating, preventing, or ameliorating a disease, disorder, or condition in a mammal having undesired copper levels that cause or lead to tissue damage (column 1, lines 22-26), including free radical or copper-involved or copper–mediated impairment of normal tissue stem cell responses (column 1, lines 26-35) where tissue damage includes endothelial dysfunction (column 12, line 67 to column 13, line 2), weakened intercellular junctions (column 13, lines 6-7), alteration of leukocyte adhesion including mononuclear leukocyte adhesion and monocyte interactions with the endothelial surface (column 13, lines 11-24) atheromatosus disorders of blood vessels and-arteries (column 28, lines 47-51), including plaque rupture of atheromatous lesions [resulting in vessel and arterial wall injury] (column 28, lines 58-61). Cooper et al., also teach accumulation of transition metals, particularly copper, in vascular tissues causes impaired tissue behavior including impaired wound repair following surgery or trauma and the exaggerated tendency to ulceration and poor healing of established ulcers (column 27, lines 18-23). Cooper et al., teach treatment with copper chelators prior to surgery by reducing excess transition metals in blood vessels (column 27, lines 27-34). Cooper et al., also teach treatment with copper chelators or other agents to remove copper in order to improve normal tissue repair processes that include the mobilization of stem cells that migrate to sites of tissue damage to effect tissue regeneration and repair, including repair of various layers of blood vessels, because repair of tissue damage is impaired or suppressed by the build up of redox-active transition metals, primarily copper, in tissues such as in the walls of blood vessels (column 27, lines 39-47). Cooper et al., teach methods of treatment and related method, uses, and pharmaceutical compositions that ameliorate, prevent or treat any one or more disease states of the cardiovascular tree and dependent organs exacerbated by elevated non-intracellular free copper. Inflammation of the cardiovascular system is taught at column 8, lines 25-20. Cooper et al., teach numerous copper chelators including tetrathiomolybdate (TTM) (column 30, lines 38-67 to column 31, lines 1-7, particularly column 30, line 62). Administration to a patient of an agent effective in lowering the copper values content of the patient's body sufficient to improve tissue repair by restoration or substantial restoration of normal tissue is taught at column 35, lines 41-43 and 55-62.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cooper et al., US Patent 6,951,890 (4 October 2005, benefit to 12 March 2002) in view of Medford et al., US Patent 5,877,203 (2 March 1999).

The claims recite a method of inhibiting cell proliferation associated with arterial wall injury comprising administering an effective amount of a copper chelator to said mammal, thereby inhibiting said cell proliferation; wherein the cell is a vascular smooth muscle cell and further wherein said copper chelator is TTM and said injury is caused by balloon angioplasty.

Cooper et al., teach methods for treating, preventing, or ameliorating a disease, disorder, or condition in a mammal having undesired copper levels that cause or lead to tissue damage (column 1, lines 22-26), including free radical or copper-involved or copper–mediated impairment of normal tissue stem cell responses (column 1, lines 26-35) where tissue damage includes endothelial dysfunction (column 12, line 67 to column 13, line 2), weakened intercellular junctions (column 13, lines 6-7), alteration of leukocyte adhesion including mononuclear leukocyte adhesion and monocyte interactions with the endothelial surface (column 13, lines 11-24) atheromatosus disorders of blood vessels and-arteries (column 28, lines 47-51), including plaque rupture of atheromatous lesions [resulting in vessel and arterial wall injury] (column 28, lines 58-61). Cooper et al., also teach accumulation of transition

metals, particularly copper, in vascular tissues causes impaired tissue behavior including impaired wound repair following surgery or trauma (column 27, lines 18-23). Cooper et al., teach treatment with copper chelators prior to surgery by reducing excess transition metals in blood vessels (column 27, lines 27-34). Cooper et al., also teach treatment with copper chelators or other agents to remove copper in order to improve normal tissue repair processes that include the mobilization of stem cells that migrate to sites of tissue damage to effect tissue regeneration and repair, including repair of various layers of blood vessels, because repair of tissue damage is impaired or suppressed by the build up of redox-active transition metals, primarily copper, in tissues such as in the walls of blood vessels (column 27, lines 39-47). Vascular smooth muscle cells are taught at column 16, line 67 to column 17, line1). Cooper et al., teach methods of treatment and related method, uses, and pharmaceutical compositions that ameliorate, prevent or treat any one or more disease states of the cardiovascular tree and dependent organs exacerbated by elevated non-intracellular free copper. Inflammation of the cardiovascular system is taught at column 8, lines 25-20. Cooper et al., teach numerous copper chelators including tetrathiomolybdate (TTM) (column 30, lines 38-67 to column 31, lines 1-7, particularly column 30, line 62). Administration to a patient of an agent effective in lowering the copper values content of the patient's body sufficient to improve tissue repair by restoration or substantial restoration of normal tissue is taught at column 35, lines 41-43 and 55-62. Cooper et al., do not each balloon angioplasty.

Medford et al., teach the administration of dithiocarboxylates and dithiocarbamates, which are well known transition metal chelators (abstract), including D-penicillamine (column 2, lines 9-13) prior to and following coronary angioplasty as a means of reducing or eliminating the abnormal proliferative and inflammatory response that frequently leads to significant restenosis (column 4, lines 41-45). Administration during use of or following use of balloon catheters is taught at column 3 lines 18-20.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Thursday 9:00am-7:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CMW